104 (New) A kit for treating cancer, comprising at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a compound comprising:

a) a chelator;

b) a targeting moiety;

c) 0-1 linking groups between the targeting moiety and chelator;

wherein the targeting moiety is an indazole nonpeptide that binds to a receptor that is upregulated during angiogenesis.

Remarks

This is a preliminary response to Continued Prosecution Application (CPA) filed herewith. After the carrying out the preliminary amendments, claims 37-50, 58-104 will be pending.

The marked-up version of amended claims is found in Appendix I, attached to this Response, and titled "Marked-Up Version of Rewritten Claims". The amendments are shown by text stricken through to indicate deletions and underlined text to indicate insertions.

Claim 58 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 58 is amended to include the material of claim 2, which has been canceled. Support for the amendment is found throughout the application, for example on page 84, lines 15-21 and page 14, line 1 to page 31, line 4. Accordingly, no new matter is added.

Claim 59 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 59 is amended to include the material of claim 2, which has been canceled. Support for the amendment is found throughout the

application, for example on page 84, lines 23-33. Accordingly, no new matter is added.

Claim 65 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 65 is amended to include the material of claim 11, which has been canceled. Support for the amendment is found throughout the application, for example on page 86, lines 28-35, and on page 12, lines 27-32. Accordingly, no new matter is added.

Claim 66 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 66 is amended to correct antecedent basis in the claim, in light of the amendment to claim 65. Support for the amendment is found throughout the application. Accordingly, no new matter is added.

Claim 67 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 67 is amended to correct antecedent basis in the claim, in light of the amendment to claim 65. Support for the amendment is found throughout the application. Accordingly, no new matter is added.

Claim 68 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 68 is amended to include the material of claim 19, which has been canceled. Support for the amendment is found throughout the application, for example on page 13, lines 25-31, page 87 lines 36 to page 88 line 5 and on page 12, lines 27-32. Accordingly, no new matter is added.

New claim 76 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example in original claim 3, and 59. Accordingly, no new matter is added.

New claim 77 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 84, lines 15-21, and page 37, line 24, to page 43, line 10. Accordingly, no new matter is added.

New claim 78 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 84, lines 15-21, and page 43, line 11 to page 44, line 15. Accordingly, no new matter is added.

New claim 79 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 84, lines 15-21, and page 45, line 1, to page 52, line 35. Accordingly, no new matter is added.

New claim 80 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 53, lines 6-8. Accordingly, no new matter is added.

New claim 81 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for on page 53, lines 10-11. Accordingly, no new matter is added.

New claim 82 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 53, lines 13-14. Accordingly, no new matter is added.

New claim 83 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, and page 57, lines 8-15. Accordingly, no new matter is added.

New claim 84 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35 and page 58, lines 1-2. Accordingly, no new matter is added.

New claim 85 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 13, line 33, to page 31, line 4. Accordingly, no new matter is added.

New claim 86 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 31, line 5, to page 37, line 23. Accordingly, no new matter is added.

New claim 87 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 37, line 24, to page 43, line 10. Accordingly, no new matter is added.

New claim 88 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 43, line 12, to page 44, line 15. Accordingly, no new matter is added.

New claim 89 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 45, line 1, to page 52, line 35. Accordingly, no new matter is added.

New claim 90 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, and page 57, lines 8-16, and page 58, lines 3-8. Accordingly, no new matter is added.

New claim 91 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 58, lines 10-14. Accordingly, no new matter is added.

New claim 92 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 58, lines 15-16. Accordingly, no new matter is added.

New claim 93 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, to page 58, line 18, to page 59, line 5. Accordingly, no new matter is added.

New claim 94 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16, page 53, lines 16-24, and page 58, lines 1-2. Accordingly, no new matter is added.

New claim 95 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16, and page 13, line 33, to page 31, line 4. Accordingly, no new matter is added.

New claim 96 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16 and page 31, line 5, to page 37, line 22. Accordingly, no new matter is added.

New claim 97 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16, and page 37, line 24, to page 43, line 10. Accordingly, no new matter is added.

New claim 98 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16, and page 43, line 12, to page 44, line 15. Accordingly, no new matter is added.

New claim 99 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16, and page 45, line 1, to page 52, line 35. Accordingly, no new matter is added.

New claim 100 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16,

and page 58, lines 4-8. Accordingly, no new matter is added.

New claim 101 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16, and page 58, lines 10-14. Accordingly, no new matter is added.

New claim 102 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16, and page 58, lines 15-16. Accordingly, no new matter is added.

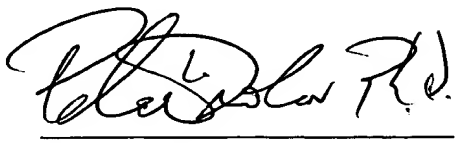
New claim 103 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16, and page 58, line 18, to page 59, line 5. Accordingly, no new matter is added.

New claim 104 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 93, lines 26-30, page 13, lines 25-31 and page 113, lines 10-18. Accordingly, no new matter is added.

Summary

Applicants submit that this application is in condition for allowance, a favorable action passing this case to issue is therefore respectfully requested. If a telephone interview would be of assistance in advancing prosecution of this application, Applicants' agent invites the Examiner to contact him at the number provided below.

Respectfully submitted,



Dated: September 7, 2001

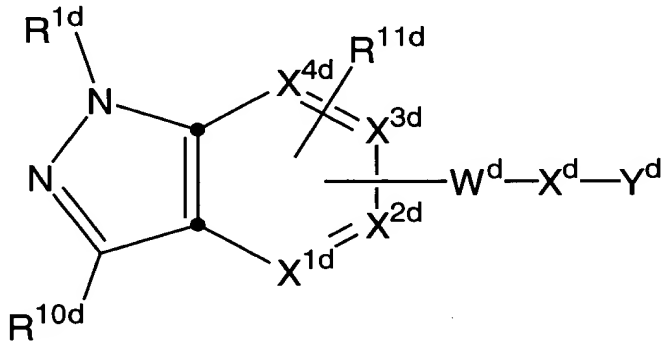
Peter L. Dolan, Ph.D.
Agent for Applicants
Registration No. 46,307
Telephone: (302)992-4528

Marked-Up Version of R writt n Claims

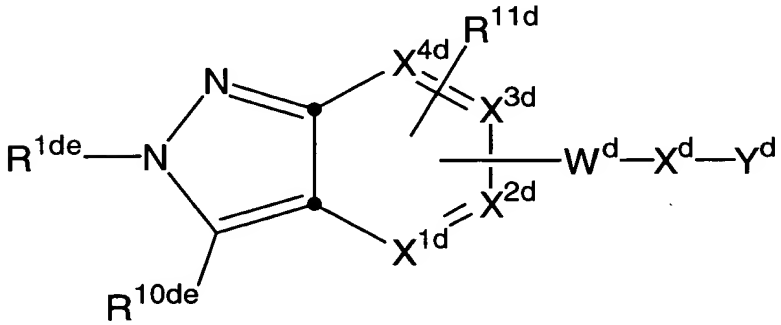
58. (Amended) A kit for treating cancer, ~~comprising a compound of~~according to Claim 104~~Claim 1~~, wherein the compound is of the formula:

$(Q)_d$-L_n-C_h or $(Q)_d$-L_n-$(C_h)_{d'}$

wherein, Q is independently a compound of Formula (Ia) or (Ib):



(Ia)



(Ib)

including stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, or pharmaceutically acceptable salt or prodrug forms thereof wherein:

X^{1d} is N, CH, C- W^d- X^d- Y^d, or C-L_n;

X^{2d} is N, CH, or C- W^d- X^d- Y^d;

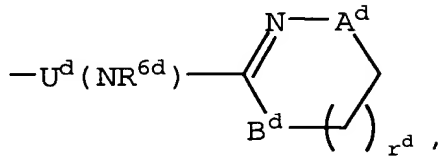
X^{3d} is N, CR^{11d}, or C- W^d- X^d- Y^d;

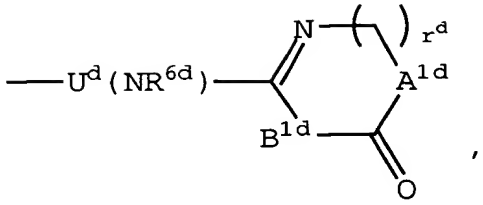
X^{4d} is N or CR^{11d};

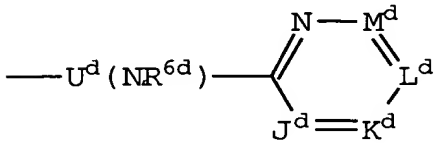
provided that when R^{1d} is R^{1de} then one of X^{1d} and X^{2d} is C- W^d- X^d- Y^d, and when R^{10d} is R^{1de} then X^{3d} is C- W^d- X^d- Y^d;

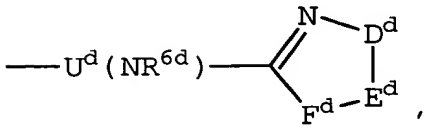
R^{1d} is selected from: R^{1de}, C_1-C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_3-C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_3-C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_4-C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d}, and aryl(C_1-C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d};

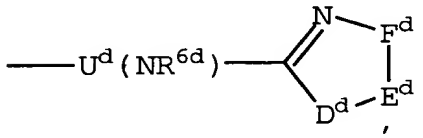
R^{1de} is selected from:

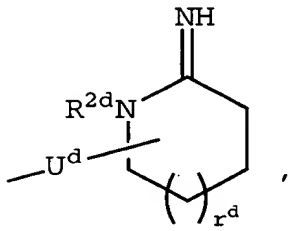

,

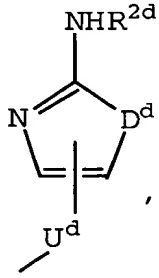

,

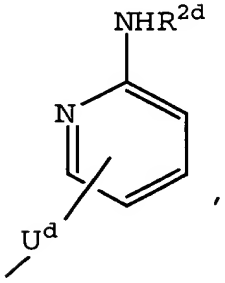

,

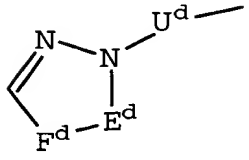

,

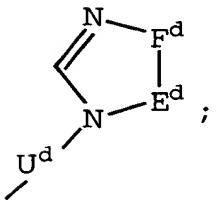

,


,


,


,


or


;

A^d and B^d are independently $-CH_2-$, $-O-$, $-N(R^{2d})-$, or $-C(=O)-$;

A^{1d} and B^{1d} are independently $-CH_2-$ or $-N(R^{3d})-$;

D^d is $-N(R^{2d})-$, $-O-$, $-S-$, $-C(=O)-$ or $-SO_2-$;

E^d-F^d is $-C(R^{4d})=C(R^{5d})-$, $-N=C(R^{4d})-$, $-C(R^{4d})=N-$, or $-C(R^{4d})_2C(R^{5d})_2-$;

J^d, K^d, L^d and M^d are independently selected from $-C(R^{4d})-$, $-C(R^{5d})-$ and $-N-$, provided that at least one of J^d, K^d, L^d and M^d is not $-N-$;

R^{2d} is selected from: H, C_1-C_6 alkyl, (C_1-C_6 alkyl)carbonyl, (C_1-C_6 alkoxy)carbonyl; (C_1-C_6 alkyl)aminocarbonyl, C_3-C_6 alkenyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, heteroaryl(C_1-C_6 alkyl)carbonyl, heteroarylcarbonyl, aryl(C_1-C_6 alkyl)-, (C_1-C_6 alkyl)carbonyl-, arylcarbonyl, C_1-C_6 alkylsulfonyl, arylsulfonyl, aryl(C_1-C_6 alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl(C_1-C_6 alkyl)sulfonyl, aryloxycarbonyl, and aryl(C_1-C_6 alkoxy)carbonyl, wherein said aryl groups are substituted with 0-2 substituents selected from the group: C_1-C_4 alkyl, C_1-C_4 alkoxy, halo, CF_3, and nitro;

R^{3d} is selected from: H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, aryl(C_1-C_6 alkyl)-, and heteroaryl(C_1-C_6 alkyl)-;

R^{4d} and R^{5d} are independently selected from: H, C_1-C_4 alkoxy, $NR^{2d}R^{3d}$, halogen, NO_2, CN, CF_3, C_1-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, aryl(C_1-C_6

alkyl)-, (C_1-C_6 alkyl)carbonyl, (C_1-C_6 alkoxy)carbonyl, and arylcarbonyl, or

alternatively, when substituents on adjacent atoms, R^{4d} and R^{5d} can be taken together with the carbon atoms to which they are attached to form a 5-7 membered carbocyclic or 5-7 membered heterocyclic aromatic or non-aromatic ring system, said carbocyclic or heterocyclic ring being optionally substituted with 0-2 groups selected from: C_1-C_4 alkyl, C_1-C_4 alkoxy, halo, cyano, amino, CF_3, and NO_2;

U^d is selected from:

$-(CH_2)_n{}^d-$,

$-(CH_2)_n{}^d(CR^{7d}=CR^{8d})(CH_2)_m{}^d-$,

$-(CH_2)_n{}^d(C\equiv C)(CH_2)_m{}^d-$,

$-(CH_2)_t{}^dQ(CH_2)_m{}^d-$,

$-(CH_2)_n{}^dO(CH_2)_m{}^d-$,

$-(CH_2)_n{}^dN(R^{6d})(CH_2)_m{}^d-$,

$-(CH_2)_n{}^dC(=O)(CH_2)_m{}^d-$,

$-(CH_2)_n{}^d(C=O)N(R^{6d})(CH_2)_m{}^d-$

$-(CH_2)_n{}^dN(R^{6d})(C=O)(CH_2)_m{}^d-$, and

$-(CH_2)_n{}^dS(O)_p{}^d(CH_2)_m{}^d-$;

wherein one or more of the methylene groups in U^d is optionally substituted with R^{7d};

Q^d is selected from 1,2-cycloalkylene, 1,2-phenylene, 1,3-phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4-pyridinylene, 2,4-pyridinylene, and 3,4-pyridazinylene;

R^{6d} is selected from: H, C_1-C_4 alkyl, and benzyl;

R^{7d} and R^{8d} are independently selected from: H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, aryl(C_1-C_6 alkyl)-, and heteroaryl(C_0-C_6 alkyl)-;

R^{10d} is selected from: H, R^{1de}, C_1-C_4 alkoxy substituted with 0-1 R^{21d}, $N(R^{6d})_2$, halogen, NO_2, CN, CF_3, CO_2R^{17d}, $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, $-SO_2R^{17d}$, $-SO_2NR^{17d}R^{20d}$, C_1-C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_3-C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_3-C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_4-C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d}, and aryl(C_1-C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d};

R^{10de} is selected from: H, C_1-C_4 alkoxy substituted with 0-1 R^{21d}, $N(R^{6d})_2$, halogen, NO_2, CN, CF_3, CO_2R^{17d}, $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, $-SO_2R^{17d}$, $-SO_2NR^{17d}R^{20d}$, C_1-C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_3-C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_3-C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_4-C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d}, and aryl(C_1-C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d};

R^{11d} is selected from H, halogen, CF_3, CN, NO_2, hydroxy, $NR^{2d}R^{3d}$, C_1-C_4 alkyl substituted with 0-1 R^{21d}, C_1-C_4 alkoxy substituted with 0-1 R^{21d}, aryl substituted with 0-1 R^{21d}, aryl(C_1-C_6 alkyl)- substituted with 0-1 R^{21d},

(C_1-C_4 alkoxy)carbonyl substituted with 0-1 R^{21d}, (C_1-C_4 alkyl)carbonyl substituted with 0-1 R^{21d}, C_1-C_4 alkylsulfonyl substituted with 0-1 R^{21d}, and C_1-C_4 alkylaminosulfonyl substituted with 0-1 R^{21d};

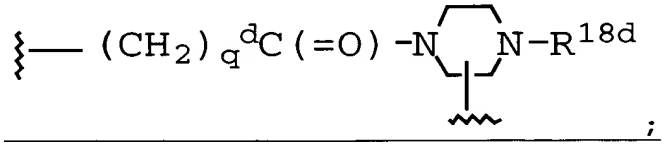
W^d is selected from:

$-(C(R^{12d})_2)_q{}^dC(=O)N(R^{13d})-$, and

$-C(=O)-N(R^{13d})-(C(R^{12d})_2)_q{}^d-$;

X^d is $-C(R^{12d})(R^{14d})-C(R^{12d})(R^{15d})-$; or

alternatively, W^d and X^d can be taken together to be



;

R^{12d} is selected from H, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_4-C_{10} cycloalkylalkyl, (C_1-C_4 alkyl)carbonyl, aryl, and aryl(C_1-C_6 alkyl)-;

R^{13d} is selected from H, C_1-C_6 alkyl, C_3-C_7 cycloalkylmethyl, and aryl(C_1-C_6 alkyl)-;

R^{14d} is selected from:

H, C_1-C_6 alkylthio(C_1-C_6 alkyl)-, aryl(C_1-C_{10} alkylthioalkyl)-, aryl(C_1-C_{10} alkoxyalkyl)-, C_1-C_{10} alkyl, C_1-C_{10} alkoxyalkyl, C_1-C_6 hydroxyalkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkylalkyl, aryl(C_1-C_6 alkyl)-, heteroaryl(C_1-C_6 alkyl)-, aryl, heteroaryl, CO_2R^{17d}, $C(=O)R^{17d}$, and $CONR^{17d}R^{20d}$, provided that any of the above alkyl, cycloalkyl, aryl or

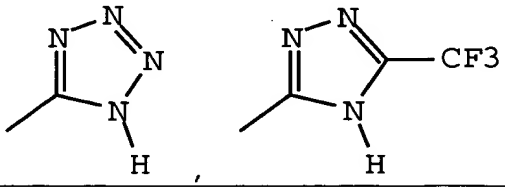
heteroaryl groups may be unsubstituted or substituted independently with 0-1 R^{16d} or 0-2 R^{11d};

R^{15d} is selected from:

H, R^{16d}, C_1-C_{10} alkyl, C_1-C_{10} alkoxyalkyl, C_1-C_{10} alkylaminoalkyl, C_1-C_{10} dialkylaminoalkyl, (C_1-C_{10} alkyl)carbonyl, aryl(C_1-C_6 alkyl)carbonyl, C_1-C_{10} alkenyl, C_1-C_{10} alkynyl ,C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkylalkyl, aryl(C_1-C_6 alkyl)-, heteroaryl(C_1-C_6 alkyl)-, aryl, heteroaryl, CO_2R^{17d}, $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, SO_2R^{17d}, and $SO_2NR^{17d}R^{20d}$, provided that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 0-2 R^{11d};

Y^d is selected from:

$-COR^{19d}$, $-SO_3H$, $-PO_3H$, tetrazolyl, $-CONHNHSO_2CF_3$, $-CONHSO_2R^{17d}$, $-CONHSO_2NHR^{17d}$, $-NHCOCF_3$, $-NHCONHSO_2R^{17d}$, $-NHSO_2R^{17d}$, $-OPO_3H_2$, $-OSO_3H$, $-PO_3H_2$, $-SO_3H$, $-SO_2NHCOR^{17d}$, $-SO_2NHCO_2R^{17d}$,



, , and ;

R^{16d} is selected from:

$-N(R^{20d})-C(=O)-O-R^{17d}$,

$-N(R^{20d})-C(=O)-R^{17d}$,

$-N(R^{20d})-C(=O)-NH-R^{17d}$,

$-N(R^{20d})SO_2-R^{17d}$, and

$-N(R^{20d})SO_2-NR^{20d}R^{17d}$;

R^{17d} is selected from:

C_1-C_{10} alkyl optionally substituted with a bond to L_n, C_3-C_{11} cycloalkyl optionally substituted with a bond to L_n, aryl(C_1-C_6 alkyl)- optionally substituted with a bond to L_n, (C_1-C_6 alkyl)aryl optionally substituted with a bond to L_n, heteroaryl(C_1-C_6 alkyl)- optionally substituted with a bond to L_n, (C_1-C_6 alkyl)heteroaryl optionally substituted with a bond to L_n, biaryl(C_1-C_6 alkyl)- optionally substituted with a bond to L_n, heteroaryl optionally substituted with a bond to L_n, aryl optionally substituted with a bond to L_n, biaryl optionally substituted with a bond to L_n, and a bond to L_n, wherein said aryl, biaryl or heteroaryl groups are also optionally substituted with 0-3 substituents selected from the group consisting of: C_1-C_4 alkyl, C_1-C_4 alkoxy, aryl, heteroaryl, halo, cyano, amino, CF_3, and NO_2;

R^{18d} is selected from:

-H,

$-C(=O)-O-R^{17d}$,

$-C(=O)-R^{17d}$,

$-C(=O)-NH-R^{17d}$,

$-SO_2-R^{17d}$, and

$-SO_2-NR^{20d}R^{17d}$;

R^{19d} is selected from: hydroxy, C_1-C_{10} alkyloxy, C_3-C_{11} cycloalkyloxy, aryloxy, aryl(C_1-C_6 alkoxy)-, C_3-C_{10} alkylcarbonyloxyalkyloxy, C_3-C_{10} alkoxycarbonyloxyalkyloxy, C_2-C_{10} alkoxycarbonylalkyloxy, C_5-C_{10} cycloalkylcarbonyloxyalkyloxy, C_5-C_{10} cycloalkoxycarbonyloxyalkyloxy, C_5-C_{10} cycloalkoxycarbonylalkyloxy,

C_7-C_{11} aryloxycarbonylalkyloxy,
C_8-C_{12} aryloxycarbonyloxyalkyloxy,
C_8-C_{12} arylcarbonyloxyalkyloxy,
C_5-C_{10} alkoxyalkylcarbonyloxyalkyloxy, C_5-C_{10} (5-alkyl-1,3-dioxa-cyclopenten-2-one-yl)methyloxy, C_{10}-C_{14} (5-aryl-1,3-dioxa-cyclopenten-2-one-yl)methyloxy, and
$(R^{11d})(R^{12d})N$-(C_1-C_{10} alkoxy)-;

R^{20d} is selected from: H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, aryl(C_1-C_6 alkyl)-, and heteroaryl(C_1-C_6 alkyl)-;

R^{21d} is selected from: COOH and NR^{6d}_2;

m^d is 0-4;

n^d is 0-4;

t^d is 0-4;

p^d is 0-2;

q^d is 0-2; and

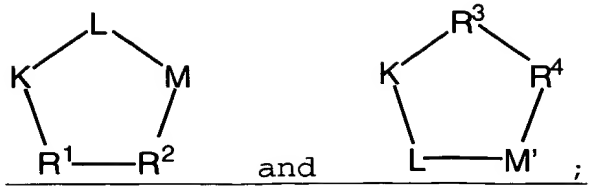
r^d is 0-2;

with the following provisos:

(1) t^d, n^d, m^d and q^d are chosen such that the number of atoms connecting R^{1d} and Y^d is in the range of 10-14; and

(2) n^d and m^d are chosen such that the value of n^d plus m^d is greater than one unless U^d is
$-(CH_2)_t{}^d Q^d (CH_2)_m{}^d-$;

or Q is a peptide selected from the group:



;

R^1 is L-valine, D-valine or L-lysine optionally substituted on the ε amino group with a bond to L_n;

R^2 is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid or tyrosine, the tyrosine optionally substituted on the hydroxy group with a bond to L_n;

R^3 is D-valine;

R^4 is D-tyrosine substituted on the hydroxy group with a bond to L_n;

provided that one of R^1 and R^2 in each Q is substituted with a bond to L_n, and further provided that when R^2 is 2-aminothiazole-4-acetic acid, K is N-methylarginine;

provided that at least one Q is a compound of Formula (Ia) or (Ib);

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

d' is 1-100;

L_n is a linking group having the formula:

$((W)_h-(CR^6R^7)_g)_x-(Z)_k-((CR^{6a}R^{7a})_{g'}-(W)_{h'})_{x'}$;

W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^8C(=O)$, $C(=O)N\ R^8$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, SO_2NH, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{10}, C_{3-10} cycloalkyl substituted with 0-3 R^{10}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{10};

R^6, R^{6a}, R^7, R^{7a}, and R^8 are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, PO_3H, C_1-C_5 alkyl substituted with 0-3 R^{10}, aryl substituted with 0-3 R^{10}, benzyl substituted with 0-3 R^{10}, and C_1-C_5 alkoxy substituted with 0-3 R^{10}, $NHC(=O)R^{11}$, $C(=O)NHR^{11}$, $NHC(=O)NHR^{11}$, NHR^{11}, R^{11}, and a bond to C_h;

R^{10} is independently selected at each occurrence from the group: a bond to C_h, $COOR^{11}$, $C(=O)NHR^{11}$, $NHC(=O)R^{11}$, OH, NHR^{11}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{11}, C_{1-5} alkyl substituted with 0-1 R^{12}, C_{1-5} alkoxy substituted with 0-1 R^{12}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{11};

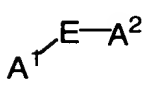
R^{11} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{12}, aryl

substituted with 0-1 R^{12}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{12}, C_{3-10} cycloalkyl substituted with 0-1 R^{12}, polyalkylene glycol substituted with 0-1 R^{12}, carbohydrate substituted with 0-1 R^{12}, cyclodextrin substituted with 0-1 R^{12}, amino acid substituted with 0-1 R^{12}, polycarboxyalkyl substituted with 0-1 R^{12}, polyazaalkyl substituted with 0-1 R^{12}, and peptide substituted with 0-1 R^{12}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to C_h;

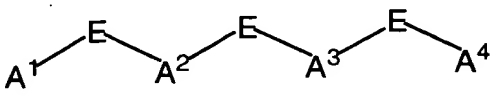
R^{12} is a bond to C_h;

k is selected from 0, 1, and 2;
h is selected from 0, 1, and 2;
h' is selected from 0, 1, and 2;
g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
x is selected from 0, 1, 2, 3, 4, and 5;
x' is selected from 0, 1, 2, 3, 4, and 5;

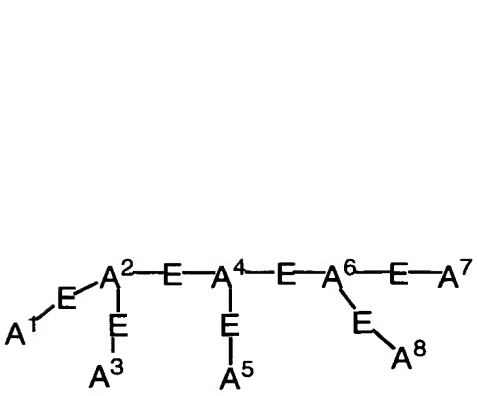
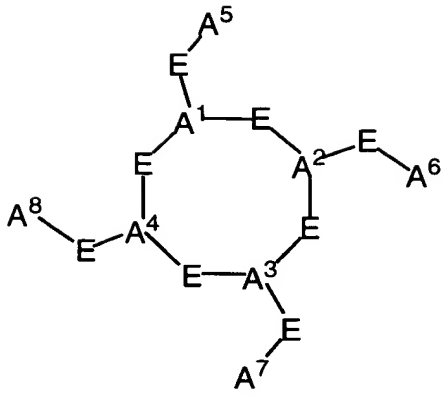
C_h is a metal bonding unit having a formula selected from the group:



,



,

, and ;

A^1, A^2, A^3, A^4, A^5, A^6, A^7, and A^8 are independently selected at each occurrence from the group: NR^{13}, $NR^{13}R^{14}$, S, SH, S(Pg), O, OH, PR^{13}, $PR^{13}R^{14}$, $P(O)R^{15}R^{16}$, and a bond to L_n;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group: C_1-C_{10} alkyl substituted with 0-3 R^{17}, aryl substituted with 0-3 R^{17}, C_{3-10} cycloalkyl substituted with 0-3 R^{17}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{17}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{17}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{17}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{13} and R^{14} are each independently selected from the group: a bond to L_n, hydrogen, C_1-C_{10} alkyl substituted with 0-3 R^{17}, aryl substituted with 0-3 R^{17}, C_{1-10} cycloalkyl substituted with 0-3 R^{17}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{17}, wherein the heterocyclo group

is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{17}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{17}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17}, and an electron, provided that when one of R^{13} or R^{14} is an electron, then the other is also an electron;

alternatively, R^{13} and R^{14} combine to form $=C(R^{20})(R^{21})$;

R^{15} and R^{16} are each independently selected from the group: a bond to L_n, -OH, C_1-C_{10} alkyl substituted with 0-3 R^{17}, C_1-C_{10} alkyl substituted with 0-3 R^{17}, aryl substituted with 0-3 R^{17}, C_{3-10} cycloalkyl substituted with 0-3 R^{17}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{17}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{17}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{17}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: a bond to L_n, =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{18}$, $-C(=O)R^{18}$, $-C(=O)N(R^{18})_2$, -CHO, $-CH_2OR^{18}$, $-OC(=O)R^{18}$, $-OC(=O)OR^{18a}$, $-OR^{18}$, $-OC(=O)N(R^{18})_2$, $-NR^{19}C(=O)R^{18}$, $-NR^{19}C(=O)OR^{18a}$, $-NR^{19}C(=O)N(R^{18})_2$,

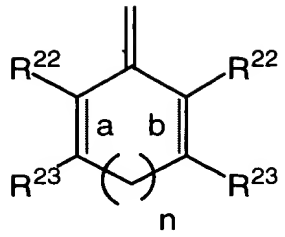
$-NR^{19}SO_2N(R^{18})_2$, $-NR^{19}SO_2R^{18a}$, $-SO_3H$, $-SO_2R^{18a}$, $-SR^{18}$, $-S(=O)R^{18a}$, $-SO_2N(R^{18})_2$, $-N(R^{18})_2$, $-NHC(=S)NHR^{18}$, $=NOR^{18}$, NO_2, $-C(=O)NHOR^{18}$, $-C(=O)NHNR^{18}R^{18a}$, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy, C_1-C_5 alkyl, C_2-C_4 alkenyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylmethyl, C_2-C_6 alkoxyalkyl, aryl substituted with 0-2 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

R^{18}, R^{18a}, and R^{19} are independently selected at each occurrence from the group: a bond to L_n, H, C_1-C_6 alkyl, phenyl, benzyl, C_1-C_6 alkoxy, halide, nitro, cyano, and trifluoromethyl;

Pg is a thiol protecting group;

R^{20} and R^{21} are independently selected from the group: H, C_1-C_{10} alkyl, -CN, $-CO_2R^{25}$, $-C(=O)R^{25}$, $-C(=O)N(R^{25})_2$, C_2-C_{10} 1-alkene substituted with 0-3 R^{23}, C_2-C_{10} 1-alkyne substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, unsaturated 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and unsaturated C_{3-10} carbocycle substituted with 0-3 R^{23};

alternatively, R^{20} and R^{21}, taken together with the divalent carbon radical to which they are attached form:



R^{22} and R^{23} are independently selected from the group: H, R^{24}, C_1-C_{10} alkyl substituted with 0-3 R^{24}, C_2-C_{10} alkenyl substituted with 0-3 R^{24}, C_2-C_{10} alkynyl substituted with 0-3 R^{24}, aryl substituted with 0-3 R^{24}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{24}, and C_{3-10} carbocycle substituted with 0-3 R^{24};

alternatively, R^{22}, R^{23} taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

a and **b** indicate the positions of optional double bonds and **n** is 0 or 1;

R^{24} is independently selected at each occurrence from the group: =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{25}$, $-C(=O)R^{25}$, $-C(=O)N(R^{25})_2$, $-N(R^{25})_3^+$, $-CH_2OR^{25}$, $-OC(=O)R^{25}$, $-OC(=O)OR^{25a}$, $-OR^{25}$, $-OC(=O)N(R^{25})_2$, $-NR^{26}C(=O)R^{25}$, $-NR^{26}C(=O)OR^{25a}$, $-NR^{26}C(=O)N(R^{25})_2$, $-NR^{26}SO_2N(R^{25})_2$, $-NR^{26}SO_2R^{25a}$, $-SO_3H$, $-SO_2R^{25a}$, $-SR^{25}$, $-S(=O)R^{25a}$, $-SO_2N(R^{25})_2$, $-N(R^{25})_2$, $=NOR^{25}$, $-C(=O)NHOR^{25}$, $-OCH_2CO_2H$, and 2-(1-morpholino)ethoxy; and,

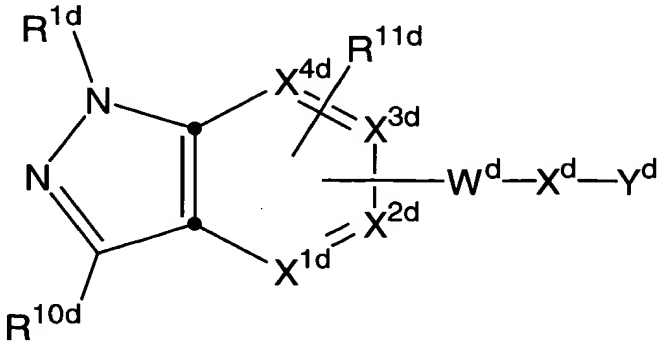
R^{25}, R^{25a}, and R^{26} are each independently selected at each occurrence from the group: hydrogen and C_1-C_6 alkyl.

~~or a pharmaceutically acceptable salt thereof, and at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.~~

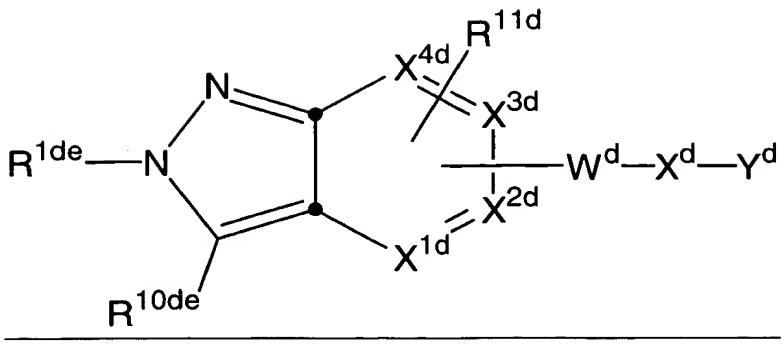
59. (Amended) A kit according to claim 58 wherein said kit comprises a plurality of separate containers, wherein at least one of said containers ~~contains a compound of Claim 1, or a pharmaceutically acceptable salt thereof, and at least another of said containers~~ contains one or more agents selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, and another of said containers contains a compound of formula:

$(Q)_d$-L_n-C_h or $(Q)_d$-L_n-$(C_h)_{d'}$

wherein, Q is independently a compound of Formula (Ia) or (Ib):



(Ia)



(Ib)

including stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, or pharmaceutically acceptable salt or prodrug forms thereof wherein:

X^{1d} is N, CH, C- W^d- X^d- Y^d, or C-L_n;

X^{2d} is N, CH, or C- W^d- X^d- Y^d;

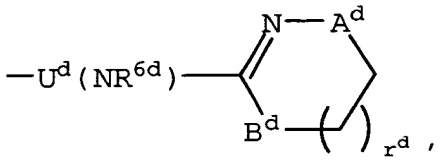
X^{3d} is N, CR^{11d}, or C- W^d- X^d- Y^d;

X^{4d} is N or CR^{11d};

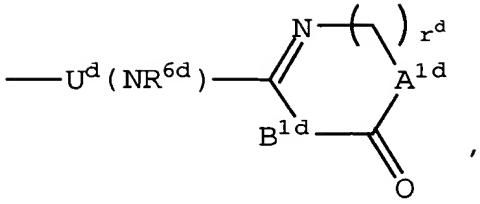
provided that when R^{1d} is R^{1de} then one of X^{1d} and X^{2d} is C- W^d- X^d- Y^d, and when R^{10d} is R^{1de} then X^{3d} is C- W^d- X^d- Y^d;

R^{1d} is selected from: R^{1de}, C_1-C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_3-C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_3-C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_4-C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d}, and aryl(C_1-C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d};

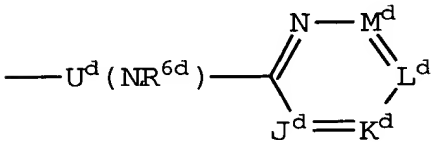
R^{1de} is selected from:



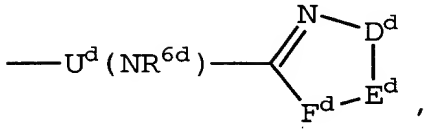
,



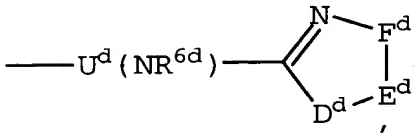
,



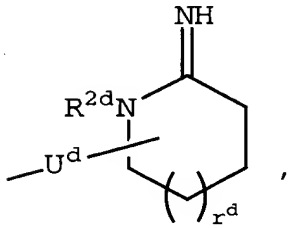
,



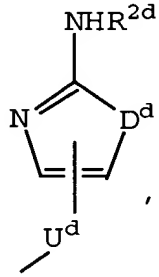
,



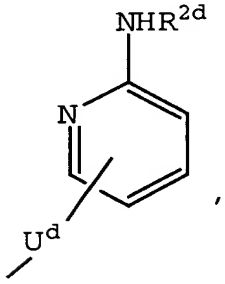
,



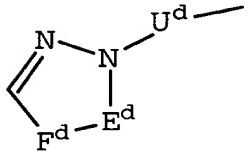
,



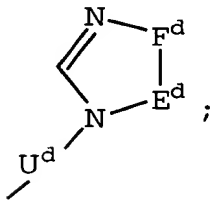
,



,



or



;

A^d and B^d are independently $-CH_2-$, $-O-$, $-N(R^{2d})-$, or $-C(=O)-$;

A^{1d} and B^{1d} are independently $-CH_2-$ or $-N(R^{3d})-$;

D^d is $-N(R^{2d})-$, $-O-$, $-S-$, $-C(=O)-$ or $-SO_2-$;

E^d-F^d is $-C(R^{4d})=C(R^{5d})-$, $-N=C(R^{4d})-$, $-C(R^{4d})=N-$, or $-C(R^{4d})_2C(R^{5d})_2-$;

J^d, K^d, L^d and M^d are independently selected from $-C(R^{4d})-$, $-C(R^{5d})-$ and $-N-$, provided that at least one of J^d, K^d, L^d and M^d is not $-N-$;

R^{2d} is selected from: H, C_1-C_6 alkyl, (C_1-C_6 alkyl)carbonyl, (C_1-C_6 alkoxy)carbonyl; (C_1-C_6 alkyl)aminocarbonyl, C_3-C_6 alkenyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, heteroaryl(C_1-C_6 alkyl)carbonyl, heteroarylcarbonyl, aryl(C_1-C_6 alkyl)-, (C_1-C_6 alkyl)carbonyl-, arylcarbonyl, C_1-C_6 alkylsulfonyl, arylsulfonyl, aryl(C_1-C_6 alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl(C_1-C_6 alkyl)sulfonyl, aryloxycarbonyl, and aryl(C_1-C_6 alkoxy)carbonyl, wherein said aryl groups are substituted with 0-2 substituents selected from the group: C_1-C_4 alkyl, C_1-C_4 alkoxy, halo, CF_3, and nitro;

R^{3d} is selected from: H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, aryl(C_1-C_6 alkyl)-, and heteroaryl(C_1-C_6 alkyl)-;

R^{4d} and R^{5d} are independently selected from: H, C_1-C_4 alkoxy, $NR^{2d}R^{3d}$, halogen, NO_2, CN, CF_3, C_1-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, aryl(C_1-C_6

alkyl)-, (C_1-C_6 alkyl)carbonyl, (C_1-C_6 alkoxy)carbonyl, and arylcarbonyl, or

alternatively, when substituents on adjacent atoms, R^{4d} and R^{5d} can be taken together with the carbon atoms to which they are attached to form a 5-7 membered carbocyclic or 5-7 membered heterocyclic aromatic or non-aromatic ring system, said carbocyclic or heterocyclic ring being optionally substituted with 0-2 groups selected from: C_1-C_4 alkyl, C_1-C_4 alkoxy, halo, cyano, amino, CF_3, and NO_2;

U^d is selected from:

$-(CH_2)_n{}^d-$,

$-(CH_2)_n{}^d(CR^{7d}=CR^{8d})(CH_2)_m{}^d-$,

$-(CH_2)_n{}^d(C\equiv C)(CH_2)_m{}^d-$,

$-(CH_2)_t{}^dQ(CH_2)_m{}^d-$,

$-(CH_2)_n{}^dO(CH_2)_m{}^d-$,

$-(CH_2)_n{}^dN(R^{6d})(CH_2)_m{}^d-$,

$-(CH_2)_n{}^dC(=O)(CH_2)_m{}^d-$,

$-(CH_2)_n{}^d(C=O)N(R^{6d})(CH_2)_m{}^d-$

$-(CH_2)_n{}^dN(R^{6d})(C=O)(CH_2)_m{}^d-$, and

$-(CH_2)_n{}^dS(O)_p{}^d(CH_2)_m{}^d-$;

wherein one or more of the methylene groups in U^d is optionally substituted with R^{7d};

Q^d is selected from 1,2-cycloalkylene, 1,2-phenylene, 1,3-phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4-pyridinylene, 2,4-pyridinylene, and 3,4-pyridazinylene;

R^{6d} is selected from: H, C_1-C_4 alkyl, and benzyl;

R^{7d} and R^{8d} are independently selected from: H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, aryl(C_1-C_6 alkyl)-, and heteroaryl(C_0-C_6 alkyl)-;

R^{10d} is selected from: H, R^{1de}, C_1-C_4 alkoxy substituted with 0-1 R^{21d}, $N(R^{6d})_2$, halogen, NO_2, CN, CF_3, CO_2R^{17d}, $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, $-SO_2R^{17d}$, $-SO_2NR^{17d}R^{20d}$, C_1-C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_3-C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_3-C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_4-C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d}, and aryl(C_1-C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d};

R^{10de} is selected from: H, C_1-C_4 alkoxy substituted with 0-1 R^{21d}, $N(R^{6d})_2$, halogen, NO_2, CN, CF_3, CO_2R^{17d}, $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, $-SO_2R^{17d}$, $-SO_2NR^{17d}R^{20d}$, C_1-C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_3-C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_3-C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C_4-C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d}, and aryl(C_1-C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d};

R^{11d} is selected from H, halogen, CF_3, CN, NO_2, hydroxy, $NR^{2d}R^{3d}$, C_1-C_4 alkyl substituted with 0-1 R^{21d}, C_1-C_4 alkoxy substituted with 0-1 R^{21d}, aryl substituted with 0-1 R^{21d}, aryl(C_1-C_6 alkyl)- substituted with 0-1 R^{21d},

(C_1-C_4 alkoxy)carbonyl substituted with 0-1 R^{21d}, (C_1-C_4 alkyl)carbonyl substituted with 0-1 R^{21d}, C_1-C_4 alkylsulfonyl substituted with 0-1 R^{21d}, and C_1-C_4 alkylaminosulfonyl substituted with 0-1 R^{21d};

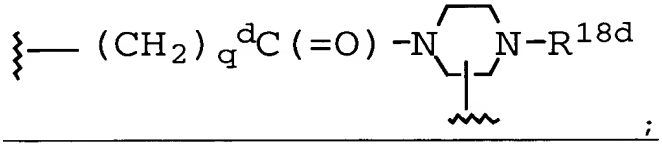
W^d is selected from:

$-(C(R^{12d})_2)_q{}^dC(=O)N(R^{13d})-$, and

$-C(=O)-N(R^{13d})-(C(R^{12d})_2)_q{}^d-$;

X^d is $-C(R^{12d})(R^{14d})-C(R^{12d})(R^{15d})-$; or

alternatively, W^d and X^d can be taken together to be



;

R^{12d} is selected from H, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_4-C_{10} cycloalkylalkyl, (C_1-C_4 alkyl)carbonyl, aryl, and aryl(C_1-C_6 alkyl)-;

R^{13d} is selected from H, C_1-C_6 alkyl, C_3-C_7 cycloalkylmethyl, and aryl(C_1-C_6 alkyl)-;

R^{14d} is selected from:

H, C_1-C_6 alkylthio(C_1-C_6 alkyl)-, aryl(C_1-C_{10} alkylthioalkyl)-, aryl(C_1-C_{10} alkoxyalkyl)-, C_1-C_{10} alkyl, C_1-C_{10} alkoxyalkyl, C_1-C_6 hydroxyalkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkylalkyl, aryl(C_1-C_6 alkyl)-, heteroaryl(C_1-C_6 alkyl)-, aryl, heteroaryl, CO_2R^{17d}, $C(=O)R^{17d}$, and $CONR^{17d}R^{20d}$, provided that any of the above alkyl, cycloalkyl, aryl or

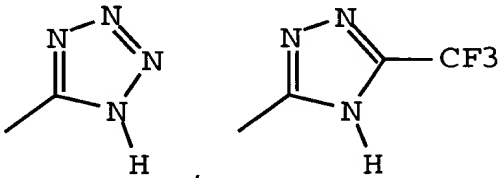
heteroaryl groups may be unsubstituted or substituted independently with 0-1 R^{16d} or 0-2 R^{11d};

R^{15d} is selected from:

H, R^{16d}, C_1-C_{10} alkyl, C_1-C_{10} alkoxyalkyl, C_1-C_{10} alkylaminoalkyl, C_1-C_{10} dialkylaminoalkyl, (C_1-C_{10} alkyl)carbonyl, aryl(C_1-C_6 alkyl)carbonyl, C_1-C_{10} alkenyl, C_1-C_{10} alkynyl ,C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkylalkyl, aryl(C_1-C_6 alkyl)-, heteroaryl(C_1-C_6 alkyl)-, aryl, heteroaryl, CO_2R^{17d}, $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, SO_2R^{17d}, and $SO_2NR^{17d}R^{20d}$, provided that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 0-2 R^{11d};

Y^d is selected from:

$-COR^{19d}$, $-SO_3H$, $-PO_3H$, tetrazolyl, $-CONHNHSO_2CF_3$, $-CONHSO_2R^{17d}$, $-CONHSO_2NHR^{17d}$, $-NHCOCF_3$, $-NHCONHSO_2R^{17d}$, $-NHSO_2R^{17d}$, $-OPO_3H_2$, $-OSO_3H$, $-PO_3H_2$, $-SO_3H$, $-SO_2NHCOR^{17d}$, $-SO_2NHCO_2R^{17d}$,



, , and ;

R^{16d} is selected from:

$-N(R^{20d})-C(=O)-O-R^{17d}$,

$-N(R^{20d})-C(=O)-R^{17d}$,

$-N(R^{20d})-C(=O)-NH-R^{17d}$,

$-N(R^{20d})SO_2-R^{17d}$, and

$-N(R^{20d})SO_2-NR^{20d}R^{17d}$;

R^{17d} is selected from:

C_1-C_{10} alkyl optionally substituted with a bond to L_n, C_3-C_{11} cycloalkyl optionally substituted with a bond to L_n, aryl(C_1-C_6 alkyl)- optionally substituted with a bond to L_n, (C_1-C_6 alkyl)aryl optionally substituted with a bond to L_n, heteroaryl(C_1-C_6 alkyl)- optionally substituted with a bond to L_n, (C_1-C_6 alkyl)heteroaryl optionally substituted with a bond to L_n, biaryl(C_1-C_6 alkyl)- optionally substituted with a bond to L_n, heteroaryl optionally substituted with a bond to L_n, aryl optionally substituted with a bond to L_n, biaryl optionally substituted with a bond to L_n, and a bond to L_n, wherein said aryl, biaryl or heteroaryl groups are also optionally substituted with 0-3 substituents selected from the group consisting of: C_1-C_4 alkyl, C_1-C_4 alkoxy, aryl, heteroaryl, halo, cyano, amino, CF_3, and NO_2;

R^{18d} is selected from:

-H,

$-C(=O)-O-R^{17d}$,

$-C(=O)-R^{17d}$,

$-C(=O)-NH-R^{17d}$,

$-SO_2-R^{17d}$, and

$-SO_2-NR^{20d}R^{17d}$;

R^{19d} is selected from: hydroxy, C_1-C_{10} alkyloxy, C_3-C_{11} cycloalkyloxy, aryloxy, aryl(C_1-C_6 alkoxy)-, C_3-C_{10} alkylcarbonyloxyalkyloxy, C_3-C_{10} alkoxycarbonyloxyalkyloxy, C_2-C_{10} alkoxycarbonylalkyloxy, C_5-C_{10} cycloalkylcarbonyloxyalkyloxy, C_5-C_{10} cycloalkoxycarbonyloxyalkyloxy, C_5-C_{10} cycloalkoxycarbonylalkyloxy,

C_7-C_{11} aryloxycarbonylalkyloxy,
C_8-C_{12} aryloxycarbonyloxyalkyloxy,
C_8-C_{12} arylcarbonyloxyalkyloxy,
C_5-C_{10} alkoxyalkylcarbonyloxyalkyloxy, C_5-C_{10} (5-alkyl-1,3-dioxa-cyclopenten-2-one-yl)methyloxy, C_{10}-C_{14} (5-aryl-1,3-dioxa-cyclopenten-2-one-yl)methyloxy, and
$(R^{11d})(R^{12d})N$-(C_1-C_{10} alkoxy)-;

R^{20d} is selected from: H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, aryl(C_1-C_6 alkyl)-, and heteroaryl(C_1-C_6 alkyl)-;

R^{21d} is selected from: COOH and NR^{6d}_2;

m^d is 0-4;

n^d is 0-4;

t^d is 0-4;

p^d is 0-2;

q^d is 0-2; and

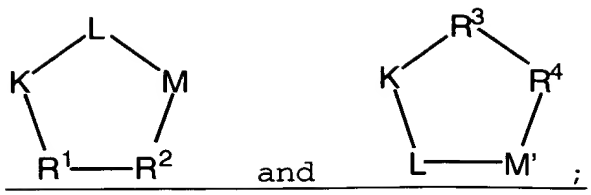
r^d is 0-2;

with the following provisos:

(1) t^d, n^d, m^d and q^d are chosen such that the number of atoms connecting R^{1d} and Y^d is in the range of 10-14; and

(2) n^d and m^d are chosen such that the value of n^d plus m^d is greater than one unless U^d is
$-(CH_2)_t{}^d\,Q^d\,(CH_2)_m{}^d-$;

or Q is a peptide selected from the group:



;

R^1 is L-valine, D-valine or L-lysine optionally substituted on the ε amino group with a bond to L_n;

R^2 is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid or tyrosine, the tyrosine optionally substituted on the hydroxy group with a bond to L_n;

R^3 is D-valine;

R^4 is D-tyrosine substituted on the hydroxy group with a bond to L_n;

provided that one of R^1 and R^2 in each Q is substituted with a bond to L_n, and further provided that when R^2 is 2-aminothiazole-4-acetic acid, K is N-methylarginine;

provided that at least one Q is a compound of Formula (Ia) or (Ib);

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

d' is 1-100;

L_n is a linking group having the formula:

$((W)_h-(CR^6R^7)_g)_x-(Z)_k-((CR^{6a}R^{7a})_{g'}-(W)_{h'})_{x'}$;

W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^8C(=O)$, $C(=O)N\ R^8$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, SO_2NH, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{10}, C_{3-10} cycloalkyl substituted with 0-3 R^{10}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{10};

R^6, R^{6a}, R^7, R^{7a}, and R^8 are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, PO_3H, C_1-C_5 alkyl substituted with 0-3 R^{10}, aryl substituted with 0-3 R^{10}, benzyl substituted with 0-3 R^{10}, and C_1-C_5 alkoxy substituted with 0-3 R^{10}, $NHC(=O)R^{11}$, $C(=O)NHR^{11}$, $NHC(=O)NHR^{11}$, NHR^{11}, R^{11}, and a bond to C_h;

R^{10} is independently selected at each occurrence from the group: a bond to C_h, $COOR^{11}$, $C(=O)NHR^{11}$, $NHC(=O)R^{11}$, OH, NHR^{11}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{11}, C_{1-5} alkyl substituted with 0-1 R^{12}, C_{1-5} alkoxy substituted with 0-1 R^{12}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{11};

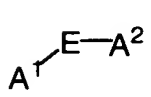
R^{11} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{12}, aryl

substituted with 0-1 R^{12}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{12}, C_{3-10} cycloalkyl substituted with 0-1 R^{12}, polyalkylene glycol substituted with 0-1 R^{12}, carbohydrate substituted with 0-1 R^{12}, cyclodextrin substituted with 0-1 R^{12}, amino acid substituted with 0-1 R^{12}, polycarboxyalkyl substituted with 0-1 R^{12}, polyazaalkyl substituted with 0-1 R^{12}, and peptide substituted with 0-1 R^{12}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to C_h;

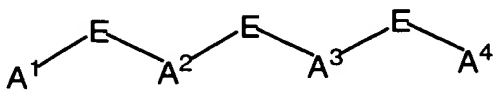
R^{12} is a bond to C_h;

k is selected from 0, 1, and 2;
h is selected from 0, 1, and 2;
h' is selected from 0, 1, and 2;
g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
x is selected from 0, 1, 2, 3, 4, and 5;
x' is selected from 0, 1, 2, 3, 4, and 5;

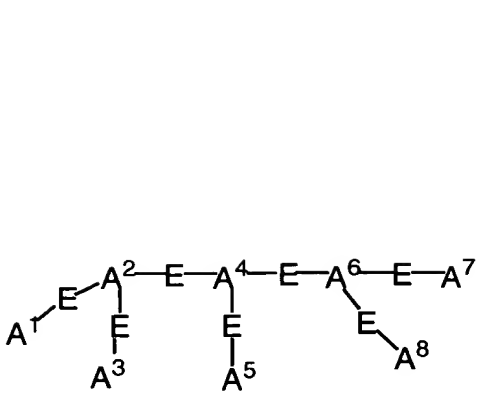
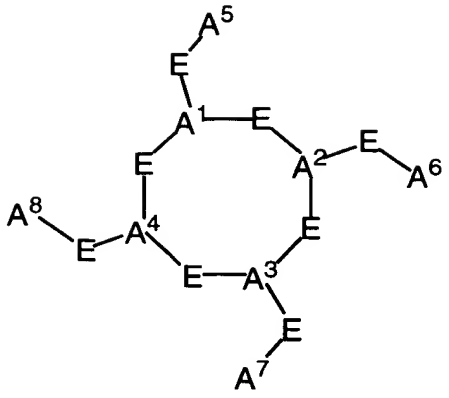
C_h is a metal bonding unit having a formula selected from the group:



,



,

, and ;

A^1, A^2, A^3, A^4, A^5, A^6, A^7, and A^8 are independently selected at each occurrence from the group: NR^{13}, $NR^{13}R^{14}$, S, SH, S(Pg), O, OH, PR^{13}, $PR^{13}R^{14}$, $P(O)R^{15}R^{16}$, and a bond to L_n;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group: C_1-C_{10} alkyl substituted with 0-3 R^{17}, aryl substituted with 0-3 R^{17}, C_{3-10} cycloalkyl substituted with 0-3 R^{17}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{17}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{17}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{17}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{13} and R^{14} are each independently selected from the group: a bond to L_n, hydrogen, C_1-C_{10} alkyl substituted with 0-3 R^{17}, aryl substituted with 0-3 R^{17}, C_{1-10} cycloalkyl substituted with 0-3 R^{17}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{17}, wherein the heterocyclo group

is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{17}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{17}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17}, and an electron, provided that when one of R^{13} or R^{14} is an electron, then the other is also an electron;

alternatively, R^{13} and R^{14} combine to form $=C(R^{20})(R^{21})$;

R^{15} and R^{16} are each independently selected from the group: a bond to L_n, -OH, C_1-C_{10} alkyl substituted with 0-3 R^{17}, C_1-C_{10} alkyl substituted with 0-3 R^{17}, aryl substituted with 0-3 R^{17}, C_{3-10} cycloalkyl substituted with 0-3 R^{17}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{17}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{17}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{17}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: a bond to L_n, =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{18}$, $-C(=O)R^{18}$, $-C(=O)N(R^{18})_2$, -CHO, $-CH_2OR^{18}$, $-OC(=O)R^{18}$, $-OC(=O)OR^{18a}$, $-OR^{18}$, $-OC(=O)N(R^{18})_2$, $-NR^{19}C(=O)R^{18}$, $-NR^{19}C(=O)OR^{18a}$, $-NR^{19}C(=O)N(R^{18})_2$,

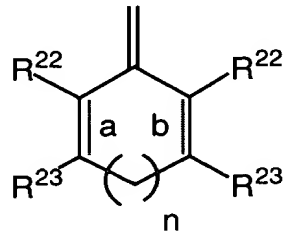
$-NR^{19}SO_2N(R^{18})_2$, $-NR^{19}SO_2R^{18a}$, $-SO_3H$, $-SO_2R^{18a}$, $-SR^{18}$, $-S(=O)R^{18a}$, $-SO_2N(R^{18})_2$, $-N(R^{18})_2$, $-NHC(=S)NHR^{18}$, $=NOR^{18}$, NO_2, $-C(=O)NHOR^{18}$, $-C(=O)NHNR^{18}R^{18a}$, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy, C_1-C_5 alkyl, C_2-C_4 alkenyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylmethyl, C_2-C_6 alkoxyalkyl, aryl substituted with 0-2 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

R^{18}, R^{18a}, and R^{19} are independently selected at each occurrence from the group: a bond to L_n, H, C_1-C_6 alkyl, phenyl, benzyl, C_1-C_6 alkoxy, halide, nitro, cyano, and trifluoromethyl;

Pg is a thiol protecting group;

R^{20} and R^{21} are independently selected from the group: H, C_1-C_{10} alkyl, -CN, $-CO_2R^{25}$, $-C(=O)R^{25}$, $-C(=O)N(R^{25})_2$, C_2-C_{10} 1-alkene substituted with 0-3 R^{23}, C_2-C_{10} 1-alkyne substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, unsaturated 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and unsaturated C_{3-10} carbocycle substituted with 0-3 R^{23};

alternatively, R^{20} and R^{21}, taken together with the divalent carbon radical to which they are attached form:



R^{22} and R^{23} are independently selected from the group: H, R^{24}, C_1-C_{10} alkyl substituted with 0-3 R^{24}, C_2-C_{10} alkenyl substituted with 0-3 R^{24}, C_2-C_{10} alkynyl substituted with 0-3 R^{24}, aryl substituted with 0-3 R^{24}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{24}, and C_{3-10} carbocycle substituted with 0-3 R^{24};

alternatively, R^{22}, R^{23} taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

a and **b** indicate the positions of optional double bonds and **n** is 0 or 1;

R^{24} is independently selected at each occurrence from the group: =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{25}$, $-C(=O)R^{25}$, $-C(=O)N(R^{25})_2$, $-N(R^{25})_3^+$, $-CH_2OR^{25}$, $-OC(=O)R^{25}$, $-OC(=O)OR^{25a}$, $-OR^{25}$, $-OC(=O)N(R^{25})_2$, $-NR^{26}C(=O)R^{25}$, $-NR^{26}C(=O)OR^{25a}$, $-NR^{26}C(=O)N(R^{25})_2$, $-NR^{26}SO_2N(R^{25})_2$, $-NR^{26}SO_2R^{25a}$, $-SO_3H$, $-SO_2R^{25a}$, $-SR^{25}$, $-S(=O)R^{25a}$, $-SO_2N(R^{25})_2$, $-N(R^{25})_2$, $=NOR^{25}$, $-C(=O)NHOR^{25}$, $-OCH_2CO_2H$, and 2-(1-morpholino)ethoxy; and,

R^{25}, R^{25a}, and R^{26} are each independently selected at each occurrence from the group: hydrogen and C_1-C_6 alkyl.

65. (Amended) A therapeutic ~~metallopharmaceutical~~ radiopharmaceutical composition comprising at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a radiopharmaceutical comprising:

a) a therapeutic metal; and

b) a compound;

wherein the compound comprises:

i) a chelator capable of chelating the therapeutic metal;

ii) a targeting moiety; and

iii) 0-1 linking groups between the targeting moiety and chelator; or

a pharmaceutically acceptable salt thereof,

wherein the targeting moiety is an indazole nonpeptide that binds to a receptor that is upregulated during angiogenesis.

~~according to claim 11, wherein the metallopharmaceutical is a therapeutic radiopharmaceutical, further comprising at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.~~

66. (Amended) A therapeutic radio~~metallo~~pharmaceutical composition according to claim 65, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetrorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin,

nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitiostanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

67. (Amended) A therapeutic radio~~metallo~~pharmaceutical composition according to claim 65, wherein radiosensitizer agent is selected from the group consiting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

68. (Amended) A method of treating cancer in a patient comprising: administering to a patient in need thereof a therapeutic radiopharmaceutical and at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof wherein the therapeutic radiopharmaceutical comprises:

a) a therapeutic metal; and

b) a compound;

wherein the compound comprises:

i) a chelator capable of chelating the therapeutic metal;

ii) a targeting moiety; and

iii) 0-1 linking groups between the targeting moiety and chelator; or

a pharmaceutically acceptable salt thereof;
wherein the targeting moiety is an indazole non-peptide that binds to a receptor that is upregulated during angiogenesis. ~~of Claim 19 or a pharmaceutically acceptable salt thereof, and at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof~~.